- **Volume status** (pulmonary capillary wedge pressure [PCWP]) PCWP above 18 mmHg correlates with congestion and an elevated preload
- **Perfusion** (CO): cardiac index of CI below 2.2 L/min/m^2 is consistent with hypoperfusion reduced contractility.

- **Subsets of acute decompensated heart failure**

1) Subset I (Warm and Dry)

- CI greater than 2.2 L/min/m2, PCWP <18 mmHg. Patients considered well compensated and perfused, without evidence of congestion. No immediate interventions necessary except optimizing oral medications and monitoring

2) Subset II (Warm and Wet)

- CI greater than 2.2 L/min/m^2, PCWP ≥18 mm Hg. Patients adequately perfused and display signs and symptoms of congestion. Main goal is to reduce preload (PCWP) carefully with loop diuretics and vasodilators

3) Subset III (Cool and Dry)

- CI less than 2.2 L/min/m^2, PCWP less than 18 mm Hg. Patients are inadequately perfused and not congested. Hypoperfusion leads to increased mortality, elevating death rates fourfold compared with those who are adequately perfused. Treatment focuses on increasing CO with positive inotropic agents and/or replacing intravascular fluids. Fluid replacement must be performed cautiously because patients can rapidly become congested

4) Subset IV (Cool and Wet)

- CI less than 2.2 L/min/m^2, PCWP greater than 18 mm Hg
- Patients are inadequately perfused and congested. Classified as the most complicated clinical presentation of AHF with the worst prognosis. Most challenging to treat; therapy targets alleviating signs and symptoms of congestion by increasing CI as well as reducing PCWP while maintaining adequate mean arterial pressure. Treatment involves a delicate balance between diuretics, vasodilators, and inotropic agents. Use of vasopressors is sometimes necessary to maintain BP

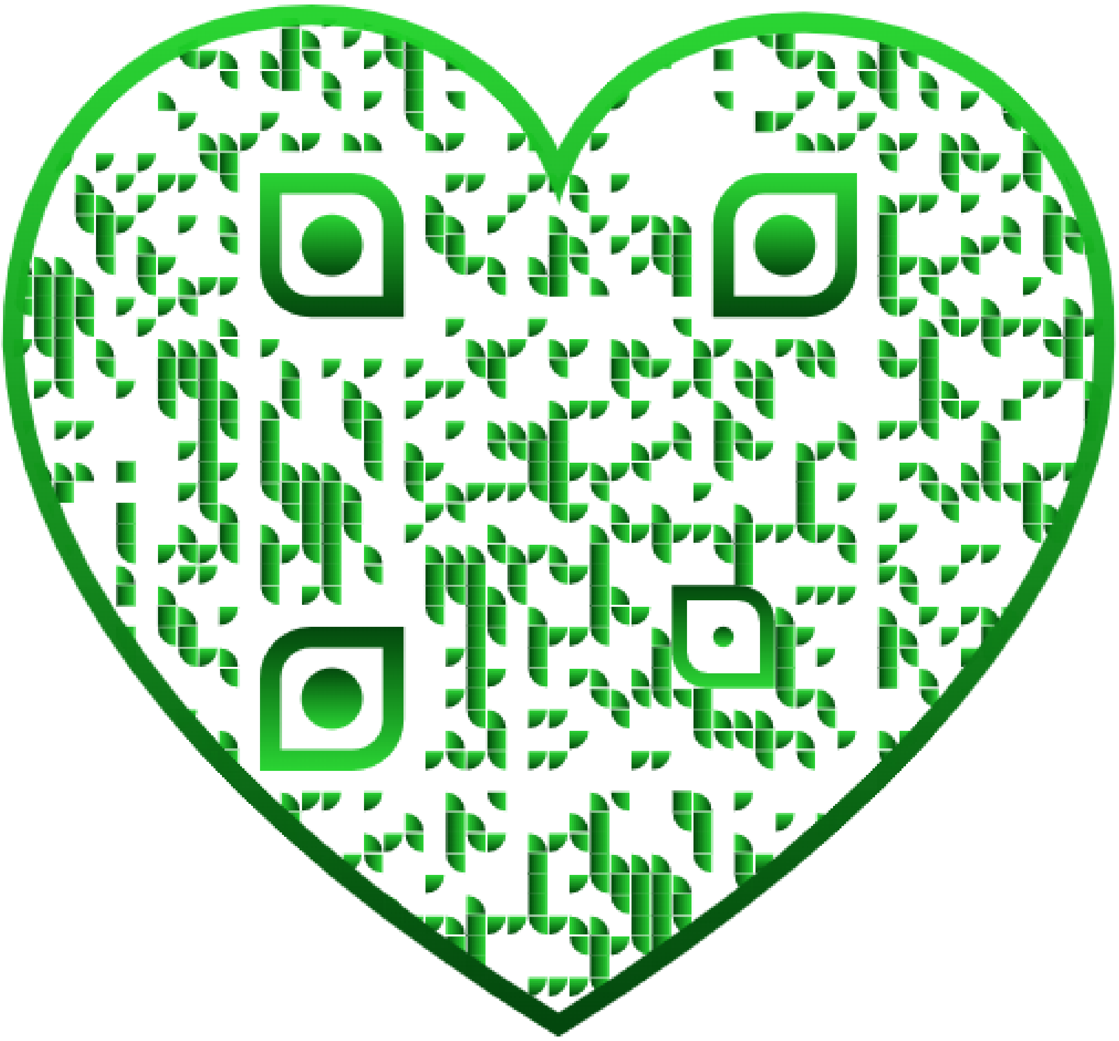

Table 4.13 AHF therapy based on hemodynamic subset[1]

Subset and description	Treatment
Subset I: Warm and Dry (normal parameters) (PCWP 15–18 mmHg and CI > 2.2 L/min/m^2)	Optimize oral medications
Subset II: Warm and Wet (pulmonary or peripheral congestion) (PCWP > 18 mmHg and CI >2.2 L/min/m^2)	**IV diuretics** ± IV vasodilators (venous) If symptoms persist, adjunct strategies to overcome diuretic resistance may be necessary.
Subset III: Cold and Dry (hypoperfusion ± orthostasis) (PCWP 15–18 mmHg and CI < 2.2 L/min/m^2)	If PCWP < 15 mm Hg, IVF until PCWP = 15–18 mm Hg. If PCWP ≥ 15 mm Hg, SBP <90 mmHg, IV inotrope. If PCWP ≥ 15 mmHg, SBP ≥90 mmHg, IV vasodilator (arterial) ±IV vasopressore if needed
Subset IV: Cold and Wet (pulmonary/peripheral congestion + hypoperfusion) (PCWP >18 mmHg and CI < 2.2 L/min/m^2).	**IV diuretics** + If SBP ≥90 mmHg, IV vasodilator (arterial) If SBP <90 mmHg, IV inotrope ±IV vasopressore if needed

CI: Cardiac ind, PCWP: pulmonary capillary wedge pressure

4.3. Atrial Fibrillation

- AF is an irregularly irregular supraventricular rhythm with no discernible, consistent atrial activity (P waves). Ventricular rate is usually 120 -180 bpm and the pulse is irregular. AF has the following ECG characteristics. The RR intervals follow no repetitive pattern. They have been labeled as "irregularly irregular." There are no distinct P waves. Atrial rate greater than 300 beats per minute
- **Prevalence**: most common arrhythmia: 2.2 million Americans. The prevalence of AF increases with advancing age; roughly 8% of patients between the ages of 80 and 89 years have AF Common comorbidity in patients with valvular heart disease or HF

✍ Symptoms

- Potential symptoms include: palpitations, chest pain, dyspenia, fatigue, lightheadedness

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[1] Bondi DS, Bridgeman MM, Burke JM, et al. **Updates in Therapeutics®: Pharmacotherapy Preparatory Review and Recertification Course**, 2021 ed. Lenexa, KS: American College of Clinical Pharmacy, 2021

✍ Classification:

a) ***Paroxysmal***: Spontaneous self-termination within 7 days of onset
b) ***Persistent***: Lasting more than 7 days
c) ***Long-standing persistent***: Continuous duration of more than 12 months
d) ***Permanent***: Present all the time, unable to return to SR using pharmacologic or non-pharmacologicoptions
e) ***Nonvalvular***: The absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair

✍ Causes of Atrial Fibrillation

- **Atrial Distension**
  - ✓ Chronic hypertension
  - ✓ Mitral valve disease
  - ✓ Cardiomyopathy
  - ✓ Congental defects
  - ✓ Pulmonary hypertension
  - ✓ Acute pulmonary embolus
  - ✓ Sleep apnea
  - ✓ Emphysema or other lung diseases
- **High adrenergic tone**
  - ✓ Alcohol withdrawal
  - ✓ Thyrotoxicosis
  - ✓ Sepsis
  - ✓ Binge drinking
  - ✓ Surgery
  - ✓ Sympathomimetics (cocaine, amphetamine)
  - ✓ Excessive theophylline, caffeine

✍ Pathophysiology

- AF may be caused by both abnormal impulse formation and abnormal impulse conduction. AF is triggered by electrical impulses generated within the pulmonary veins. These impulses initiate the process of reentry within the atria, and AF is believed to be sustained by multiple reentrant wavelets operating simultaneously within the atria. AF leads to electrical remodeling of the atria. Therefore, it is often said that "atrial fibrillation begets atrial fibrillation"; that is, AF causes atrial electrophysiologic alterations that further promote AF
- A substantial amount of the atrial electrical activity occurring during AF is conducted through the AV node into the ventricles, resulting in ventricular rates ranging from 100 to 200 beats/min
- AF is associated with substantial morbidity and mortality. This arrhythmia is associated with a risk of ischemic stroke of approximately 5% per year. The risk of stroke is increased two to seven-fold in patients with AF compared to patients without this arrhythmia. AF is the cause of roughly one of every six strokes. Patients with AF are also at increased risk for systemic thromboembolism. AF is associated with a threefold increase in the risk of HF as a result of tachycardia-induced cardiomyopathy

✍ Management of AF

- **Goals of therapy**
  - ✓ Ventricular rate control;
  - ✓ Termination of AF and restoration of sinus rhythm ("cardioversion" or "conversion to sinus rhythm");
  - ✓ Maintenance of sinus rhythm, or reduction in the frequency of episodes of paroxysmal AF; and/or
  - ✓ Prevention of stroke and systemic thromboembolism

(1) Ventricular rate control

- ✓ Ventricular rate control can be achieved by inhibiting the proportion of electrical impulses conducted from the atria to the ventricles through the AV node. If patients have a rapid ventricular rate, AV nodal blockade is necessary. Goal HR is resting HR less than 80 beats/minute. A more lenient rate control (resting HR less than 110 beats/minute) may be reasonable in patients who are asymptomatic and have LVEF preserved.

i) β-Blockers

- ✓ Any agent with β-blockade can be used and dosed to the goal HR
- ✓ *Labetalol* or *carvedilol* if additional α1-blockade is desirable (e.g., HTN)
- ✓ Can be considered in patients with stable HFrEF (only carvedilol, metoprolol succinate, or bisoprolol)

ii) Non-DHP CCBs: Verapamil or diltiazem

- ✓ Avoid use if there is concomitant systolic dysfunction.
- ✓ May be preferred over β-blocker in patients with asthma or severe chronic obstructive pulmonary disease

iii) Digoxin

- ✓ Often **ineffective alone** for controlling ventricular rate in AF, especially during exercise or movement (because of minimal effectiveness with sympathetic stimulation). It can be included in regimen if patient has HFrEF. It might be effective if additional HR control is needed when a patient is already receiving a β-blocker, diltiazem, or verapamil
- ✓ IV: 0.25 mg every 2 hours, up to 1.5 mg over 24 hours
- ✓ PO maintenance: 0.125–0.25 mg once daily

iv) Amiodarone

- ✓ May be used for rate control in patients who are refractory to other therapies such asβ-blockers, non-DHP CCBs, and digoxin

(2) Rhythm control

- Inspecific patients with intractable and intolerable symptoms (dyspnea and palpitations) despite adequate rate control or in patients for whom adequate ventricular rate control cannot beachieved, restoration and maintenance of SR may be desirable
- Oral Antiarrhythmic Agents to Induce or Maintain SR

- ✓ Choice of agent depends on patient comorbidities

i) Class Ic antiarrhythmics: Flecainide and propafenone

- ✓ First-line therapies for patients withoutstructural heart disease
- ✓ Concomitant AV nodal blocking agent (β-blocker or non-DHP CCB) typically required
- ✓ Contraindicated in patients with structural heart disease (including CHD, HF, LVH, and valvular heart disease)

ii) Class III antiarrhythmics

a) **Amiodarone**: 85%–95% efficacy

- ✓ Dosing: Oral loading dose required (400 mg 2 or 3 times per day for 2 weeks and then400mg/day for 4 weeks, followed by a 200-mg/day maintenance dose).
- ✓ Adverse effects: hepatotoxic, hypothyroidism, visual impairment, blue skin syndrome, sun burn, tremor, neuropathy,
- ✓ Monitoring: LFT, TFT, ECG, Chest X-ray

b) **Sotalol**: 50%–60% efficacy

- ✓ Recommended starting dose is 80 mg twice daily (unless CrCl <60 mL/min, then once daily). It is renally excreted, adjust dose in renal impairment. Sotalol is contraindicated in patients with uncontrolled HF

c) **Dofetilide**: 50%–60% effcacy

- ✓ May use in patients with HF
- ✓ Contraindicated in patients with CrCl less than 20 mL/minute

d) **Dronedarone**: 21%–25% efficacy

- ✓ Amiodarone analog lacking the iodine moiety that contributes to the thyroid toxicity of amiodarone

(3) Antithrombotic therapy

- The average annual stroke rate is 5% per year without anticoagulation
  - ✓ A patient's individual risk can vary from about 1% to 20% per year depending on risk factors. Risk stratification and treatment determination is based on the **CHA_2DS_2-VASc score,** for use in patients with nonvalvular atrial fibrillation.

i) Direct Oral Anticoagulants

a) Dabigatran

- ✓ Direct Factor II (thrombin) inhibitor indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular AF; demonstrated superiority to warfarin for efficacy
- ✓ Dose:
  - ➢ CrCl > 30mL/min: 150 mg twice daily
  - ➢ CrCl 15-30mL/min: 75 mg twice daily
  - ➢ CrCl <15mL/min: no dosing recommendation available

Table 4.14 Risk stratification and anti-thrombotic treatment determination[1]

Risk factor	Score	**Recommendations for antithrombotic therapy**
CHF or LVEF ≤40%	1	**1)** CHA$_2$DS$_2$-VASc score = 0 ➲ Reasonable to omit antithrombotic therapy **2)** CHA$_2$DS$_2$-VASc score = 1 ➲ Antithrombotic therapy or aspirin or OAC may be considered **3)** CHA$_2$DS$_2$-VASc score = 2 ➲ OAC recommended NB: Maximum point value is 9
Hypertension	1	
Age > 75 years	2	
Diabetes	1	
Stroke, TIA, thromboimbolism	2	
Vascular Disease	1	
Age 60 – 74 years	1	
Sex category (female)	1	

b) Rivaroxaban

- ✓ Factor Xa inhibitor indicated to reduce the risk of stroke and systemic embolism in patientswith nonvalvular AF; demonstrated noninferiority compared with warfarin for efficacy
- ✓ Dose:
  - ➢ CrCl > 50mL/min: 20 mg once daily
  - ➢ CrCl 15-50mL/min: 15 mg once daily
  - ➢ CrCl <15mL/min: Avoid use

c) Apixaban

- ✓ Factor Xa inhibitor indicated to reduce the risk of stroke and systemic embolism in patientswith nonvalvular AF; demonstrated superiority over warfarin for efficacy
  - ➢ Dose: 5mg twice daily

d) Edoxaban

- ✓ Factor Xa inhibitor indicated to reduce the risk of stroke and systemic embolism in patientswith nonvalvular AF; demonstrated noninferiority compared with warfarin for efficacy
- ✓ Dose:
  - ➢ CrCl > 50mL/min: 60 mg once daily
  - ➢ CrCl 15-50mL/min: 30 mg once daily
  - ➢ CrCl <15mL/min: Avoid use

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[1] Friberg L, Rosenqvist M, Lip GY. **Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study.** *Eur Heart J.* 2012 Jun;33(12):1500-10

ii) Warfarin

- Inhibits vitamin K–dependent clotting factors II, VII, IX, X. Also inhibits anticoagulant proteins C and S
- Dosing: It is based on what is needed to achieve *an INR goal of 2–3* for patients with *nonvalvular AF*. For patients with mitral stenosis, prosthetic heart valves, prior thromboembolism, or persistent atrial thrombus on TEE, *an INR goal of 2.5–3.5 or even higher* may be indicated. Initial starting dose is usually *5 mg/day*. Lower starting dose (2–3 mg/day) should be considered in patients with: advanced age, low body weight, drug interactions, malnourishment, HF, hyperthyroid state, low albumin, or liver disease
  - ✓ Adjusting dose: Watch for trends; remember that the INR seen today is the result of the doses given in the past 4–5 days. It takes 5–7 days to reach full effect, given the half-lifeof factor II.
    - o Half-lives of vitamin K–dependent clotting factor VII, 6 hrs; factor IX, 24 hrs; factor X, 36 hrs; factor II, 72 hrs
    - ➢ If INR is out of therapeutic range, increase or decrease cumulative weekly warfarin doseby 5%–20% depending on INR; if INR is high, hold one or two doses and resume at alower dose.
- Adverse effect: Bleeding: incidence 2.4%–29%, life threatening 2%–8% (epistaxis, hematuria, GI hemorrhage, bleeding gums).

4.4. Dyslipidemia

✍ Introduction

- Cholesterol is a naturally occurring sterol that is essential for life.
  - ✓ Precursor molecule for the formation of bile acids (which are required for absorption of nutrients), synthesis of steroid hormones (which provide important modulating effects in the body), and formation of cell membranes
- TGs are an important source of stored energy in adipose tissue.
- Cells derive cholesterol in two ways: by intracellular synthesis or by uptake from the systemic circulation.
- One important and early step in its synthesis is the conversion of ***hydroxymethylglutaryl-coenzyme A (HMG-CoA)*** to mevalonic acid by HMG-CoA reductase enzyme

✍ Lipoproteins:

- The second way cells obtain cholesterol is by extracting it from the systemic circulation. The source of this cholesterol is the liver, where it is synthesized and secreted into the systemic circulation. Because cholesterol and other fatty substances are insoluble in water, they are formed into complexes in the hepatocyte and gut before being secreted into the aqueous medium of the blood. The three major lipoproteins found in the blood of fasting (10–12 hours) patients are very-low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL).

1) **Very-Low-Density Lipoproteins** contain 15% to 20% of the total blood cholesterol concentration and most of the total blood TG concentration. The concentration of cholesterol in these particles is approximately one fifth of the total TG concentration
2) ***Low-Density Lipoproteins*** particles carry 60% to 70% of the total blood cholesterol and make the greatest contribution to the development of atherosclerosis. Half of the LDL particles are removed from the systemic circulation by the liver; the other half may be taken up by peripheral cells or deposited in the *intimal space of coronary, carotid, and other peripheral arteries,* where *atherosclerosis* can develop.
3) **High-Density Lipoproteins** *particles transport cholesterol from peripheral cells back to the liver,* a process called *reverse cholesterol transport.*
4) **Chylomicrons** unlike the lipoproteins that transport cholesterol from the liver to peripheral cells and back (endogenous system), chylomicrons transport fatty acids and cholesterol derived from the diet or synthesized in the intestines from the gut to the liver **(exogenous system)**

✍ **Normal values in mg/dl:** Total cholesterol <200, LDL<100, HDL: 40-60, TG<150

✍ **Etiology**

- Hypercholesterolemia: hypothyrodism, obstructive liver diseases, nephrotic syndrome, drugs (e.g. progestin, thiazides, BBs, PIs)
- Hypertriglyceridemia: obesity, DM, lipodystrophy, pregnancy, acute hepatitis, SLE, drugs (e.g. alcohol, BB, thiazides, estrogen, glucocorticoids, bile acid resins.)
- Low HDL: malnutrition, obesity, drugs (e.g. progestin)

✍ **Management**

- Determine the Presence of Major Risk Factors for ASCVD

Table 4.15 Major risk factors of ASCVD

Risk Factor	Definition
Age (years)	Male ≥45; Female ≥55
Family Hx of premature CHD events	Male 1st-degree relative at < 55 years Female 1st-degree relative at < 65 years
Hypertension	SBP ≥140 mm Hg; DBP ≥90 mm Hg
HDL cholesterol	< 40 mg/dL
Cigarette smoking	Within the past month

- **ASCVD Risk Assessment and Treatment Goals**

1) Viry high risk

- ✓ ASCVD: MI or other ACS, Coronary or other revascularization procedures, TIA, ischemic stroke, atherosclerotic PAD
- ✓ DM (type 1 or 2) with ≥ 2 other major ASCVD risk factors or evidence of end-organ damage
- ✓ **Goal cholesterol**: non-HDL≤100 mg/dL, LDL ≤70 mg/dL

2) High Risk

- ✓ ≥ 3 major ASCVD risk factors
- ✓ DM (type 1 or 2) with 0–1 other major ASCVD risk factors and no evidence of end organ damage
- ✓ CKD stage 3 or 4
- ✓ LDL ≥ 190 mg/dL (severe hypercholesterolemia)
- ✓ ≥ 10% ASCVD risk
- ✓ **Cholesterol Goal:** Non-HDL < 130 mg/dL, LDL goal: < 70 mg/dL

3) Moderate risk: Two major ASCVD risk factors

- ✓ Consider drug therapy: non-HDL ≥ 160 mg/dL (goal: <130); LDL ≥ 130 mg/dL (goal: <100)

4) Low risk: 0–1 major ASCVD risk factor

- ✓ Consider drug therapy: non-HDL ≥ 190 mg/dL (goal: <130); LDL ≥ 160 mg/dL (goal: <100)

✍ **Lifestyle Modification**

1) Heart-healthy diet: consumption of fruits, vegetables, whole grains, low-fat dairy products, skinless poultry and fish, nuts and legumes, and non-tropical vegetable oils. Limit sweets, sugar-sweetened beverages, and red meats. Lower intake of saturated fats and replace with unsaturated fats
2) Regular exercise
3) Maintain healthy weight
4) Smoking cessation

✍ **Statin Therapy**

Key Concepts *statin therapy is recommended for 2^0 and 1^0 preventions at moderate - to high-intensity doses in specific benefit groups. The four major statin benefit groups are:*

1)Patients with clinical ASCVD: CHD, stroke or TIA, and PAD.
2)Patients with an LDL-C of 190 mg/dL or greater
3)Patients with DM age 40–75 years with an LDL-C of 70–189 mg/dL and without ASCVD
4)Patients age 40–75 years with an LDL-C of 70–189 mg/dL and an estimated 10-year ASCVD risk of ≥ 7.5% without DM or ASCVD

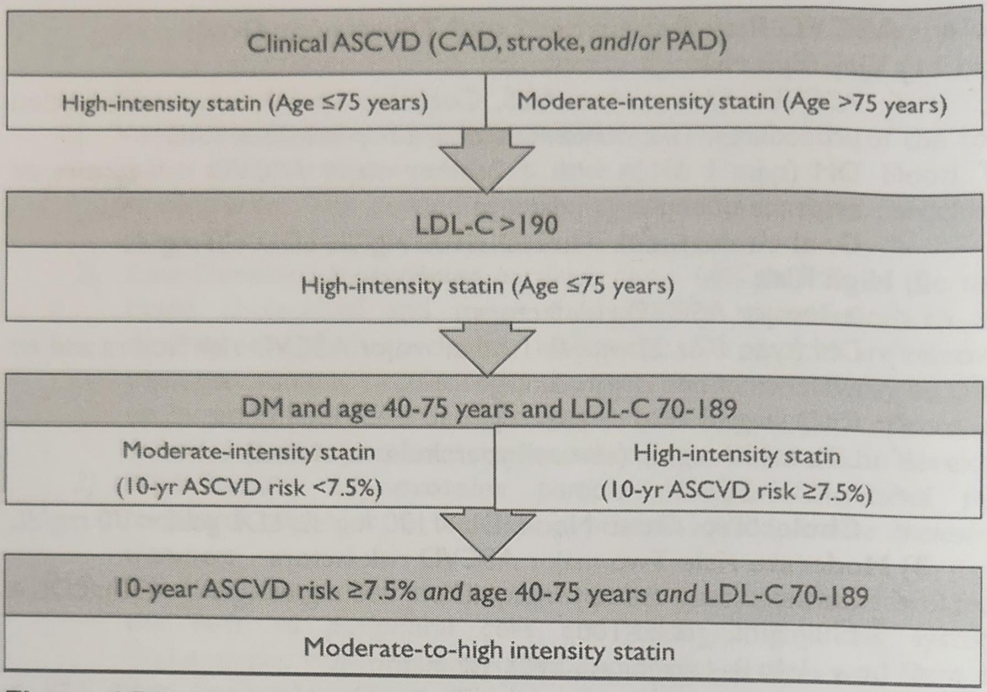
Clinical ASCVD (CAD, stroke, *and/or* PAD)
High-intensity statin (Age ≤75 years)
Moderate-intensity statin (Age >75 years)
LDL-C >190
High-intensity statin (Age ≤75 years)
DM and age 40-75 years and LDL-C 70-189
Moderate-intensity statin (10-yr ASCVD risk <7.5%)
High-intensity statin (10-yr ASCVD risk ≥7.5%)
10-year ASCVD risk ≥7.5% *and* age 40-75 years *and* LDL-C 70-189
Moderate-to-high intensity statin

Figure 4.5 Statin intensity recommendations[1]

- Main adverse effects and monitoring for statins
  - ✓ Myopathy
  - ✓ Elevated liver enzymes: LFT, symptoms of hepatic injury
  - ✓ Absolute contraindications are active liver disease, pregnancy and nursing mothers

✍ **Management of very high TG concentrations** (> 500 mg/dL)

- ✓ Primary goal is to prevent pancreatitis. Weight loss (5%–10% weight loss results in a 20% reduction in TG). Limit sugars and other simple carbohydrates, when possible.
- ✓ Exercise: Aerobic activity at least twice weekly
- ✓ Evaluate for secondary causes.
- ✓ Pharmacologic therapy: Fibrates, omega-3 fatty acids, and niacin will produce largest TG reductions. Statins can also be considered first-line therapy in patients with TG levels of 500–999 mg/dL

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[1] Bondi DS, Bridgeman MM, Burke JM, et al. **Updates in Therapeutics®: Pharmacotherapy Preparatory Review and Recertification Course**, 2021 ed. Lenexa, KS: American College of Clinical Pharmacy, 2021

Table 4.16 High, moderate, and low-intensity statin dose[1]

Atorva	Fluva	Pitava	Lova	Prava	Rosuva	Simva	%↓ in LDL
---	20-40	1	20	10-20	---	10	30
10	80	2	40	40	---	20	38
20	---	4	80	80	5	40	41
40	---	---	---	---	10	---	47
80	---	---	---	---	20	---	55
	---	---	---	---	40	---	63

■ Denotes high-intensity statin; lowers LDL-C by ≥ 50%

▩ Denotes moderate-intensity statin; lowers LDL-C by 30% to < 50%

░ Denotes low-intensity statin; lowers LDL-C by < 30%

4.5. Coronary Heart Disease

- Coronary heart disease is also called ischemic heart disease (IHD) or coronary artery disease (CAD). "**Ischemic**" refers to a decreased supply of oxygenated blood, in this case to the heart muscle. IHD results from an imbalance between **myocardial oxygen supply** and **oxygen demand.** **Angina** is discomfort in the chest that occurs when the blood supply to the myocardium is compromised.
- Common features of CHD include:
  1) Chronic stable angina
  2) Acute coronary syndromes (ACS)
     a) Unstable angina (UA)
     b) Myocardial infarction (MI): Non – ST-segment elevation MI (NSTEMI) and ST-segment elevation MI (STEMI).
- CHD is the leading cause of death for both men and women in the US.
- **Pathophysiology**
  - **Increased Myocardial O_2 Demand:** Reductions in coronary **blood flow** (secondary to atherosclerotic plaques, vasospasm, or thrombus formation) and **arterial O_2 content** (secondary to hypoxia) decrease myocardial

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[1] Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM: **2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.** *Journal of the American College of Cardiology* 2014, **63**(25 Part B):2889-2934

oxygen supply. Because the coronary arteries fill during diastole, **decreases in diastolic filling time** (e.g., tachycardia) can also reduce coronary perfusion and myocardial oxygen supply. In chronic stable angina, **atherosclerotic plaques** are the most common cause of coronary artery narrowing and reductions in coronary blood flow.

- **Decreased Myocardial O_2 Supply:** Reductions in coronary **blood flow** (secondary to atherosclerotic plaques, vasospasm, or thrombus formation) and **arterial oxygen content** (secondary to hypoxia) decrease myocardial oxygen supply. Because the coronary arteries fill during diastole, **decreases in diastolic filling time** (e.g., tachycardia) can also reduce coronary perfusion and myocardial oxygen supply. In chronic stable angina, **atherosclerotic plaques** are the most common cause of coronary artery narrowing and reductions in coronary blood flow. In contrast, in ACS, disruption of an atherosclerotic plaque with subsequent **thrombus** (blood clot) formation causes abrupt reductions in coronary blood flow and oxygen supply. **Anemia, CO poisoning**, and **cyanotic congenital heart** disease are examples of conditions that reduce the oxygen-carrying capacity of the blood, potentially causing ischemia in the face of adequate coronary perfusion.

✍ **Risk factors**

Modifiable

- Cigarette smoking
- Dyslipidemia: ↑ LDL or total cholesterol, ↓ HDL cholesterol
- Diabetes mellitus
- Hypertension
- Physical inactivity
- Obesity (BMI ≥30 kg/m^2)

Non-modifiable

- Age ≥45 yrs for males, ≥ 55 yrs for females
- Gender (men and postmenopausal women)
- Family history of premature cardiovascular disease,

✍ **Clinical Presentation and Diagnosis**

1) **Symptoms of Angina Pectoris:** Patients typically describe pain as a sensation of pressure, heaviness, or squeezing in the anterior chest area. Sharp pain is not a typical symptom of IHD. Pain may radiate to the neck, jaw, shoulder, back, or arm. Pain may be accompanied by dyspnea, nausea, vomiting, or diaphoresis. Symptoms are often **provoked by exertion** (e.g., walking, climbing stairs, and doing yard or house work) or **emotional stress** and relieved within minutes by **rest** or **nitroglycerin**. Other precipitating factors include exposure to **cold temperatures** and **heavy meals**. Pain that occurs **at rest** or that is prolonged and unrelieved by nitroglycerin is indicative of an ACS.
2) **Biochemical markers** CK, CK-MB fraction, troponin I & troponin T):
   - ✓ Elevated in MI (STEMI and non–STEMI)
   - ✓ Normal in chronic stable angina and unstable angina

3) **ECG:** Normal at rest in patients with chronic stable angina in the absence of active ischemia. Significant Q waves indicate prior MI. *ST-segment depression* or *T-wave inversion* is typically observed in chronic stable angina, unstable angina, and non–STEMI, whereas ST-segment elevation occurs with STEMI and Prinzmetal's (variant) angina

4) **Coronary Angiography:** detects the location and degree of coronary atherosclerosis

✍ Management of IHD/CSA

1) **PCI**: For patients with stable IHD, optimal medical therapy is equivalent to PCI in reducing major adverse cardiac events (MACE) and is the preferred initial strategy. PCI is indicated when: (a) when optimal medical therapy fails, (b) ymptoms are unstable, or (c) extensive coronary atherosclerosis is present (eg, greater than 70% occlusion of coronary lumen),

2) **Prevent ACS and Death**

i) Antiplatelet Agents:

- Platelets play a major role in the pathophysiology of ACS. Thromboxane A2 (TXA2) is a potent platelet activator. **Aspirin** inhibits cyclooxygenase, an enzyme responsible for the production of TXA2, thereby inhibiting platelet activation and aggregation. In patients with stable or unstable angina, aspirin has been consistently shown to reduce the risk of major adverse cardiac events, particularly MI. *Aspirin doses of 75 to 162 mg daily are recommended in patients with or at risk for IHD. If aspirin is contraindicated (eg, aspirin allergy) or is not tolerated by the patient, an alternative antiplatelet agent such as clopidogrel should be considered.*

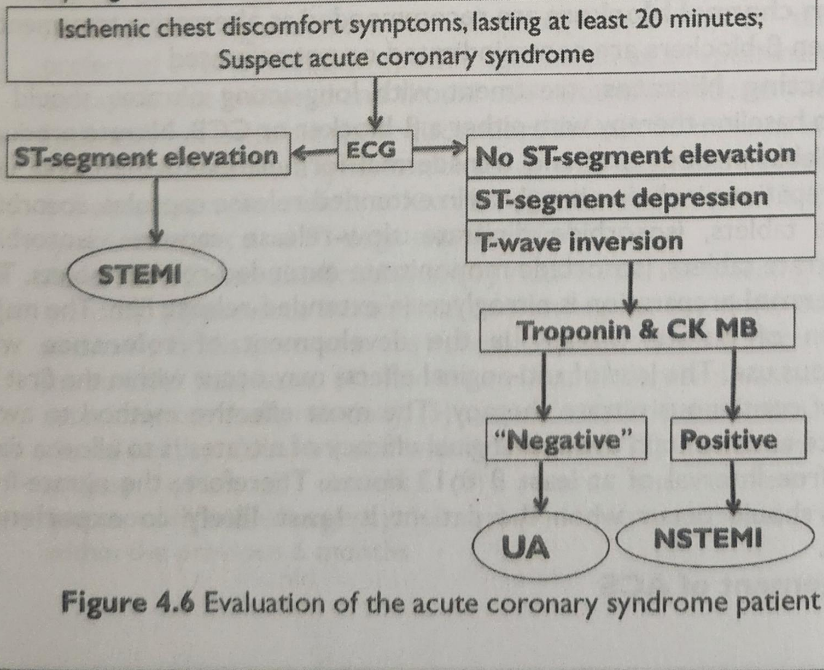
Ischemic chest discomfort symptoms, lasting at least 20 minutes;
Suspect acute coronary syndrome
ECG
ST-segment elevation
No ST-segment elevation
ST-segment depression
T-wave inversion
STEMI
Troponin & CK MB
"Negative"
Positive
UA
NSTEMI

Figure 4.6 Evaluation of the acute coronary syndrome patient

- *Inhibition of the P2Y12 receptor with either a tclopidogrel, prasugrel or ticagrelor prevents platelet aggregation and is indicated in combination with aspirin in select patients with IHD.* Dual antiplatelet therapy with aspirin and a P2Y12 inhibitor is recommended following hospitalization for ACS and/or following PCI with stent placement to prevent ischemic events. Clopidogrel is a prodrug that must be converted via a two-step process to its active thiol metabolite.

ii) **Control of Risk Factors**: dyslipidemia, hypertension, and diabetes

iii) **Statins:** should be considered in all patients with IHD, regardless of baseline LDL cholesterol

iv) **ACE-I/ARBs:** should be considered in all patients with IHD, particularly those individuals who also have hypertension, diabetes mellitus, chronic kidney disease, left ventricular dysfunction, history of MI

3) Relieve Acute Symptoms

- ***Nitroglycerin:** Should have sublingual nitroglycerin tablets or spray to relieve acute ischemic symptoms.* At the onset of an angina attack, a 0.3 to 0.4 mg dose of nitroglycerin (tablet or spray) should be administered sublingually, and repeated every 5 minutes up to three times or until symptoms resolve. Sublingual nitroglycerin may be used to prevent effort- or exertion-induced angina. In this case, the patient should use sublingual nitroglycerin 2 to 5 minutes prior to an activity known to cause angina, with the effects persisting for approximately 30 minutes

4) Prevent recurrent ischemic symptoms

- **β-blockers** are the preferred initial therapy to prevent symptoms of angina in patients with IHD because of their potential cardioprotective effects
- **Calcium channel blockers** are recommended as alternative treatment in IHD when β-blockers are contraindicated or not tolerated
- **Long-Acting Nitrates**: treatment with long-acting nitrates should be added to baseline therapy with either a β-blocker or CCB. Nitrate products are available in both oral and transdermal formulations for chronic use. **Oral** prepations include nitroglycerin extended-release capsules, sosorbide dinitrate tablets, isosorbide dinitrate slow-release capsules, isosorbide mononitrate tablets, isosorbide mononitrate extended-release tablets. The **transdermal** preparation is nitroglycerin extended-release film. The major limitation of nitrate therapy is the development of **tolerance** with continuous use. The loss of anti-anginal effects may occur within the first 24 hours of continuous nitrate therapy. The most effective method to avoid tolerance and maintain the anti-anginal efficacy of nitrates is to allow a daily nitrate-free interval of at least 8 to12 hours. Therefore, the nitrate-free interval should occur when the patient is **least likely to experience angina.**

✍ **Management of ACS**

I) Reperfusion Strategies for STEMI

- Patients with STEMI are at the highest risk of death; therefore, immediate reperfusion strategies should be initiated. Target time to initiate reperfusion treatment is within 30 minutes of hospital arrival for fibrinolytics (eg, alteplase, reteplase, and tenecteplase) and within 90 minutes from presentation for primary PCI
- Based on the risk assessment, a management strategy is chosen for NSTE ACS an invasive strategy, which involves coronary angiography, or An ischemia-guided strategy

a) PCI

- *Early reperfusion therapy with primary PCI of the infarct artery within 90 minutes from time of hospital presentation is the reperfusion treatment of choice for patients with STEMI who present within 12 hours of symptom onset.* Lower mortality rate with primary PCI as compared with fibrinolysis. More than 90% of occluded infarct-related coronary arteries are opened with primary PCI compared with fewer than 60% with fibrinolytics. Intracranial hemorrhage (ICH) and major bleeding risks from primary PCI are lower than the risks of severe bleeding events following fibrinolysis

b) Fibrinolytic Therapy

- Administration of a fibrinolytic agent is indicated in patients with STEMI who present to the hospital within 12 hours of the onset of chest discomfort. The use of fibrinolytics between 12 and 24 hours after symptom onset should be limited to patients with ongoing ischemia. It is recommended that the fibrinolytic agent be administered within 30 minutes of arrival. More fibrin-specific agents such as alteplase, reteplase, or tenecteplase is preferred over a nonfibrin-specific agent such as streptokinase. Fibrinolytic therapy is not indicated and should not be used in patients with NSTE-ACS
- **Indications**: Ischemic chest discomfort at least 20 minutes in duration but 12 hours or less since symptom onset **and** ST-segment elevation or ongoing ischemic chest discomfort at least 20 minutes in duration 12–24 hours since symptom onset **and** ST-segment elevation
- **Absolute Contraindications: (1)** Active internal bleeding (not including menses), (2) previous intracranial hemorrhage at any time; ischemic stroke within 3 months (except acute ischemic stroke within 4.5 hours), (3) known intracranial neoplasm, (4) known structural cerebral vascular lesion (eg, arteriovenous malformation), (5) suspected aortic dissection, (6) significant closed head or facial trauma within 3 months, (7) intracranial or intraspinal surgery within 2 months, (8) severe uncontrolled hypertension (unresponsive to emergency therapy) (9) for streptokinase, prior treatment within the previous 6 months

2) Early Pharmacologic Therapy

- Oxygen
- Initial Antiplatelet/ Anticoagulant Therapy
- Nitrates
- Analgesics: morphine
- Beta-Adrenergic Blockers
- Additional Therapies: Statins, ACEIs/ARBs, CCBs,

3) Secondary Prevention Following MI

- All patients should receive long-term treatment with
  - ✓ **ASA**: 81 mg daily indefinitely
  - ✓ **A β-blocker**: for 3 years (if no HF), indefinitely (if with HF)
  - ✓ **An ACE inhibitor**: in all patients
  - ✓ **A statin** for 2^0 prevention of death, stroke, or recurrent infarction
- A P2Y12 inhibitor should be continued for at least 12 months for patients undergoing PCI and for patients with NSTE-ACS receiving an ischemia-guided treatment strategy.

4.6. Stroke

- *Stroke* involves abrupt onset of focal neurologic deficit that lasts at least 24 hours and is presumed to be of vascular origin. Stroke can be either ischemic or hemorrhagic.
- Transient ischemic attacks (TIAs) are focal ischemic neurologic deficits lasting less than 24 hours and usually less than 30 minutes.
- Stroke is the third most common cause of death in the developed world after ischemic heart disease and cancer, and is the most common cause of severe physical disability. About *one-fifth* of patients with an acute stroke will die within a month of the event, and at least ½ of those who survive will be left with physical disability.
- A systematic review and meta-analysis in Ethiopia reported that the overall magnitude of hypertension, atrial fibrillation and diabetes mellitus among stroke patients were 47%, 8%, and 10%, respectively. According to this review, the overall in-hospital mortality of stroke in Ethiopia was 18%.[1]

✍ **Risk Factors**

- *Modifiable*
  - ✓ Arterial hypertension
  - ✓ TIA
  - ✓ Prior stroke
  - ✓ Carotid disease/stenosis
- *Non-modifiable*
  - ✓ Age
  - ✓ Gender
  - ✓ Race/ethnicity
  - ✓ Family history

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[1] Alene M, Assemie MA, Yismaw L, Ketema DB: **Magnitude of risk factors and in-hospital mortality of stroke in Ethiopia: a systematic review and meta-analysis**. *BMC Neurology* 2020, **20**(1):309.

- ✓ DM
- ✓ Dyslipidemia, obesity
- ✓ Smoking
- ✓ Excessive alcohol
- ✓ Genetics

✍ Classification

1) *Ischemic Stroke*
   - ✓ Ischemic strokes (87% of all strokes) are due either to local thrombus formation or emboli occluding a cerebral artery
   - ✓ In ***cardiogenic embolism***, stasis of blood flow in the atria or ventricles leads to formation of local clots that can dislodge and travel through the aorta to the cerebral circulation.
   - ✓ ***Thrombus*** formation and embolism result in arterial occlusion, decreasing cerebral blood flow and causing ischemia and ultimately infarction distal to the occlusion.
2) *Intracranial Hemorrhage:* is caused by bleeding directly into or around the brain;
   - ➢ It produces neurologic symptoms
   - ➢ By producing a mass effect on neural structures,
   - ➢ From the toxic effects of blood itself, or
   - ➢ By increasing intracranial pressure.

✍ Clinical Presentation and Diagnosis

- Weakness on one side of the body, inability to speak, loss of vision, vertigo, or falling.
- Hemiparesis, aphasia
- CT scan of the head: identifying that a hemorrhage has occurred.
- MRI: reveal areas of ischemia earlier and with better resolution than a CT scan.

✍ Treatment of Ischemic Stroke

> **Key Concepts** *All patients should have a **brain CT scan or MRI scan** to differentiate an ischemic stroke from a hemorrhagic stroke, as the treatment will differ accordingly and thrombolytic (fibrinolytic) therapy must be avoided until a hemorrhagic stroke is ruled out.*

- Identification of the time and manner of stroke onset is an important determinant in treatment.
- Supportive: blood glucose, electrolyte and volume status should be corrected
- DVT prophylaxis: Heparin 5000 units subcutaneously
- Primary prevention

- ✓ Reduction in risk factors (control of hypertension, smoking cessation, control of diabetes, cholesterol reduction)
- ✓ Treatment of atrial fibrillation

- *Acute treatment:*
  - ✓ Thrombolytic therapy (tPA 0.9 mg/kg IV over 1 hour) within 4.5 hours of onset
  - ✓ Aspirin 160–325 mg daily started within 48 hours of onset
- *Secondary prevention*
  - ✓ Non-cardioembolic
    - ➢ Aspirin 50–325 mg daily, OR
    - ➢ Aspirin 25 mg + extended-release dipyridamole 200 mg twice daily, OR
    - ➢ Clopidogrel 75 mg daily
  - ✓ Cardioembolic (especially AF)
    - ➢ Warfarin (INR = 2.5), OR
    - ➢ Apixaban 5 mg twice daily, OR
    - ➢ Dabigatran 150 mg twice daily, OR
    - ➢ Rivaroxaban 20 mg daily, OR
  - ✓ LDL > 100 mg/dL: High intensity statin therapy
  - ✓ BP control

✍ Treatment of Hemorrhagic Stroke

- Surgical
- Medical
  - ✓ Managing BP before and after aneurysm Rx
  - ✓ Seizure- prophylactic phenytoin

> **Key Concepts** *Vasospasm of the cerebral vasculature is thought to be responsible for the delayed ischemia and occurs between 4 and 21 days after the bleed.* ***Nimodipine*** *60 mg every 4 hours for 21 days is recommended*

✍ Outcome evaluation

- Monitor for the development of neurologic worsening (recurrence or extension), complications (thromboembolism, infection), and adverse treatment effects.
- Monitor bleeding for patients on aspirin and thrombolytic therapy
- For patients on warfarin: check INR and hg/hct.

4.7. Venous Thromboembolism

- ✍ VTE is manifested as deep vein thrombosis (DVT) and/or pulmonary embolism (PE)
- ✍ Results from clot formation within the venous circulation, most commonly the legs, (others: the arms, and in the mesenteric and cerebral veins)

Risk Factors

- Age: 1 in 100,000 in adolescents, 1 in 100 in old age
- History of VTE: Strongest known risk factor of DVT and PE
- Venous stasis
  - ✓ Major medical illness (e.g., CHF, status post-MI)
  - ✓ Major surgery (e.g., general anesthesia >30 minutes)
  - ✓ Paralysis and immobility (e.g., plaster casts, status post-stroke, spinal cord injury)
- Polycythemia vera
- Obesity
- Varicose veins
- Vascular injury
  - ✓ Major orthopedic surgery (knee and hip replacement)
  - ✓ Trauma (especially fractures of the pelvis, hip, or leg)
  - ✓ Indwelling venous catheters
- Hypercoagulable states
  - ✓ Malignancy
  - ✓ Genetics
  - ✓ Nephrotic syndrome
  - ✓ Pregnancy/postpartum
- Drug therapy
  - ✓ Estrogen-containing contraception
  - ✓ Estrogen replacement therapy
  - ✓ SERMs (tamoxifen)
  - ✓ Heparin-induced thrombocytopenia

Clinical Presentation and Diagnosis

DVT

- Symptoms
  - ✓ Leg swelling, pain and warmth
- Signs: dilated superficial veins, palpable cord, Homan's sign
- Lab tests: CBC, PT, INR, aPTT, RFT, LFT
- Diagnostic tests
  - ✓ US
  - ✓ Venography: Gold standard

PE

- Symptoms
  - ✓ Cough, chest pain, chest tightness, SOB, palpitation, hemoptysis
- Signs: tachypnea, diaphoretic, distended veins, cyanotic, hypotensive, hypoxia, shock
- Lab tests: CBC, AST,
- Diagnostic tests: CT scan, Pulmonary-angiography: gold standard

Prevention and Treatment of VTE

- **Prevention**
  - ✓ For hospitalized general surgical and medical patients, either of the following
    1) UFH 5000 Units every 12 or 8 hours,
    2) LMWH:
       - ➢ Enoxaparin: 40 mg SC daily,
       - ➢ Dalteparin 2500 to 5000 Units SC daily, or
    3) Fondaparinux 2.5 mg SC daily.
       - ❖ *Fondaparinux > enoxaparin/dalteparin > UFH*

- ✓ For patients following major orthopedic surgery
  1) UFH: 5000 Units every 12 or 8 hours
  2) LMWH:
     - ➢ Enoxaparin 30mg SC BID or 40 mg SC daily
     - ➢ Dalteparin 5000 Units SC daily
  3) Fondaparinux: 2.5 mg SC daily
  4) Adjusted dose warfarin (maintain an INR between 2 and 3)
  5) Rivaroxaban: 10 mg PO daily
  6) Apixaban: 2.5 mg PO daily
     - ❖ *Rivaroxaban/apixaban > LMWH > UFH/warfarin*
- ✓ **Duration of Prophylaxis**
  - ➢ Should be given throughout the period of risk.
  - ➢ For patients who have undergone total knee replacement, total hip replacement, or hip fracture repair prophylaxis is recommended for a minimum of 10 to 14 days

✍ **Treatment**

- The treatment of VTE should initially include a ***rapid-acting injectable anticoagulant*** (UFH, LMWH, fondaparinux) or a rapidly acting DOAC (eg, apixaban, rivaroxaban).

> **Key Concepts** *If warfarin is used for oral anticoagulation, it should be initiated on the same day as the parenteral anticoagulant, and the parenteral agent should be overlapped for a minimum of 5 days and until the INR is greater than or equal to 2 for at least 24 hours*

- Anticoagulation therapy should be continued for a minimum of 3 months. However, the duration of anticoagulation therapy should be based on the patient's risk of VTE recurrence and major bleeding
- For patients with cancer and women who are pregnant, the LMWHs are the preferred agents during long-term and extended treatment phases due to better safety or efficacy
- Duration: Acute: (5 – 10 days), long-term (3 months), extended (beyond 3 months)

A) Acute Phase Treatment of VTE

1) *Parenteral Anticoagulants*

a) UFH
- ✓ IV: 80 units/kg (or 5000 units) I.V. push followed by continuous infusion of 18 units/kg/hour (or alternatively 1000 units/hour)
- ✓ SC: 17,500 units (250 units/kg) given every 12 hours (after an initial 5000 unit IV bolus dose)

b) LMWHs

- ✓ Enoxaparin: 1.5 mg/kg SC once daily *or* 1 mg/kg SC twice daily; if CrCl < 30 mL/min: 1 mg/kg SC once daily
- ✓ Dalteparin: 200 units/kg SC daily *or* 100 units/kg SC twice daily

c) Factor Xa Inhibitor

- ✓ Fondaparinux:
  - ➢ Body weight < 50 kg: 5 mg SC once daily
  - ➢ Body weight 50–100 kg: 7.5 mg SC once daily
  - ➢ Body weight > 100 kg: 10 mg SC once daily

2) *Direct Oral Anticoagulants*

- ✓ Apixaban: 10 mg PO twice daily for the initial 7 days, then 5 mg po twice daily
- ✓ Rivaroxaban: 15 mg PO twice daily for the initial 21 days, then 20 mg PO daily

B) Prevention of Recurrence VTE

1) *Direct Oral Anticoagulants*

- ✓ Rivaroxaban: 20 mg once daily
- ✓ Apixaban: 2.5 mg BID

2) **Warfarin**: start with 5 mg daily and adjust dose based on INR

- ✓ Warfarin exerts its anticoagulant effect by inhibiting production of the vitamin K–dependent coagulation factors II, VII, IX, and X, as well as the anticoagulant proteins C and S.
- ✓ Warfarin has no effect on circulating coagulation factors that have been previously formed, and its therapeutic antithrombotic activity is delayed for 5 to 7 days, and potentially longer in slower metabolizers.
- ✓ This delay is related to half-lives of the clotting factors: 60 to 100 hours for factor II, 6 to 8 hours for factor VII, 20 to 30 hours for factor IX, and 24 to 40 hours for factor X.
- ✓ Proteins C and S, the ***natural anticoagulants***, are inhibited more rapidly due to their shorter half-lives, 8 to 10 hours and 40 to 60 hours, respectively.
- ✓ Warfarin does not follow linear kinetics. Small-dose adjustments can lead to large changes in anticoagulant response. The dose of warfarin is determined by each patient's individual response to therapy and the desired intensity of anticoagulation.
- ✓ For treatment and prevention of VTE, the INR target is 2.5 with an acceptable range of 2 to 3
- ✓ INR should be monitored:
  - ➢ Every 2 to 3 days during the first week of therapy.
  - ➢ Weekly for the first 1 to 2 weeks
  - ➢ Every 4 to 6 weeks thereafter

REVIEW QUESTIONS

1. A 45-year-old man with type II diabetes has blood pressures of 150/96 mm Hg on two separate occasions. Which of the following is the best initial therapy for this patient?

   A. Hydrochlorothiazide B. ACE inhibitor
   C. Beta-blocker D. Beta-blocker and HCT

   Question no. 2 and 3 pertain to the following case

   G.G. is a 56-year-old white man with type 2 diabetes. He is a nonsmoker and is concerned about his risk of CHD. His vital signs include BP 152/98 mm Hg (average home blood pressure 150/92 mm Hg), heart rate 70 beats/minute, and BMI 26.5 kg/m^2. His fasting laboratory test results today include SCr 0.8 mg/dL, total cholesterol (TC) 188 mg/dL, low-density lipoprotein cholesterol (LDL) 130 mg/dL, high-density lipoprotein cholesterol (HDL) 30 mg/dL, and triglycerides (TG) 90 mg/dL, and his urine albumin/creatinine ratio is 86.5 mg/g (previously 68 mg/g). The patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk is 21%.
2. Which is most appropriate to recommend for this patient's BP control at today's visit?
   A. Amlodipine 5 mg/day.
   B. Lisinopril 10 mg/day.
   C. Hydrochlorothiazide 12.5 mg/day plus amlodipine 5 mg/day.
   D. Chlorthalidone 12.5 mg/day plus lisinopril 10 mg/day.
3. Which is best for primary prevention of CHD for this patient?
   A. Aspirin 325 mg/day.
   B. Atorvastatin 10 mg/day.
   C. Aspirin 81 mg/day plus atorvastatin 40 mg/day.
   D. Atorvastatin 40 mg/day plus clopidogrel 75 mg/day.
4. Which pharmacological agent is *not* important in the management of CHF?
   A. Atenolol B. Metoprolol
   C. Carvedilol D. Bisoprolol
5. One of the following classes of medication is less important than the others in the management of systolic heart failure,
   A. Beta blockers B. ACE inhibitors
   C. Calcium channel blockers D. Aldosterone antagonists
6. R.R. is a 62-year-old woman with congestive heart failure is taking furosemide 80 mg orally twice daily, lisinopril 40 mg orally once daily, and metoprolol succinate 100 mg orally once daily. At her last clinic visit, her serum creatinine had increased to 2.0 mg/dL (her serum creatinine was 1.5 mg/dL 1 year ago). This change was accompanied by a 5.5 KG weight loss leaving her 2 KG less than her typical dry weight. The patient states that

she feels well. Which of the following treatment options is best for this patient?
A. Discontinue lisinopril and furosemide and recheck labs in 1 week.
B. Discontinue lisinopril and recheck labs in 1 week.
C. Discontinue furosemide and recheck labs in 1 week.
D. Continue current therapy and recheck labs in 1 week

7. J.R. is a 55-year-old man (weight 66 kg) with a medical history significant for HTN and a MI 9 months ago, leading to placement of a bare metal stent (BMS). His current medications include aspirin 325 mg/day, clopidogrel 75 mg/day, atorvastatin 40 mg/day, and metoprolol succinate 50 mg/day. His vital signs are BP 145/88 mm Hg and heart rate 52 beats/minute. His laboratory test results show LDL 68 mg/dL (baseline 138 mg/dL) and SCr 1.0 mg/dL. Which is currently best for secondary prevention of CHD?
A. Decrease the aspirin dose to 81 mg/day and add lisinopril to 5 mg/day.
B. Increase atorvastatin to 80 mg/day and increase metoprolol succinate to 100 mg/day.
C. Decrease the aspirin dose to 81 mg/day and increase metoprolol succinate to 100 mg/day.
D. Discontinue clopidogrel and increase atorvastatin to 80 mg/day.

8. B.C., a 40-year-old woman (height, 165 cm; weight, 75 kg), presents to the ED with shortness of breath and lower extremity swelling in her left leg. Her diagnosis is a new acute pulmonary embolism, which was identified on chest CT. Her medical history includes DVT 2 years ago (treated with anticoagulation therapy for 3 months and then stopped), factor V Leiden mutation, HTN, and dyslipidemia. Her medications are lisinopril 40 mg orally daily, atorvastatin 10 mg orally daily, and aspirin 81 mg orally daily. Initial laboratory values include HCT 40%, prothrombin time (PT) 9.9 seconds, INR 1.1, aPTT 30 seconds, platelet count 300,000/mm^3, and CrCl 67 mL/minute. How long should this patient be treated with anticoagulation therapy?
A. 3 months. B. 6 months. C. 12 months. D. Indefinitely.

9. B.G. is a 36-year-old man with a medical history of dyslipidemia, HPN, COPD, and HFrEF. His BP today in clinic is 128/80 mm Hg with a heart rate of 60 beats/minute. His current medication regimen includes furosemide 20 mg orally once daily, metoprolol succinate 200 mg orally once daily, atorvastatin 20 mg orally once daily, tiotropium one 18-mcg inhalation once daily, and amlodipine 5 mg orally once daily. He has a history of lisinopril-induced angioedema. Which of the following is the best modification to his medication regimen?
A. Add valsartan 80 mg orally daily.
B. Add eplerenone 50 mg orally daily.

C. Change furosemide to bumetanide 2 mg orally daily.
D. Change metoprolol succinate to carvedilol 25 mg orally twice daily

10. One of the following statements is **true** in the management of stroke
    A. Alteplase therapy is beneficial whenever it is given
    B. Patients who are taking oral warfarin are candidates for alteplase therapy
    C. Aspirin is indicated for hemorrhagic stroke
    D. Dipyridamole plus aspirin is more effective than aspirin alone
11. **True** regarding venous thromboembolism
    A. LMWHs are more effective than Fondaparinux in VTE prophylaxis
    B. Direct oral anticoagulants can be used in acute management of VTE
    C. In the long-term management of VTE warfarin should be started immediately after D/C of heparin.
    D. The minimum duration of DVT management is 10 days
12. A.M. is a 32-year-old woman with T1DM and HTN. Her current medication regimen is as follows: enalapril 10 mg/day, HCT 25 mg/day, amlodipine 10 mg/day and insulin as directed. Her vital signs today include BP 125/80 mm Hg, repeated BP 123/81 mm Hg; HR 82 beats/minute; height 168 cm; weight 70 kg. A.M. and her husband have decided they are ready to have children. What is the best medication option for A.M.?
    A. No change in therapy is warranted.
    B. Discontinue enalapril and replace with labetalol.
    C. Increase hydrochlorothiazide to 50 mg/day.
    D. Discontinue all antihypertensive therapy
13. MM. is a 63-year-old woman who just finished 6 months of diet and exercise for dyslipidemia. She has a history of gout, chronic nonischemic HF (LVEF 26%), diet-controlled DM, and asthma; she drinks 3 beers per day. No family history records are available. Her medications are albuterol metered dose inhaler, lisinopril, and furosemide. Her vital signs include BP 124/80 mm Hg and HR 75 beats/minute. Her laboratory results are: HDL-C 64 mg/dL, LDL-C 101 mg/dL, TG 98 mg/dL, and TC 185 mg/dL. Her 10-year ASCVD risk is estimated to be 7.1%. What is the most appropriate next step for M.M.?
    A. Initiate moderate-intensity statin C. Initiate high-intensity statin
    B. Initiate low-intensity statin D. Do not initiate statin therapy.
14. According to the ACC/AHA blood cholesterol guidelines, which is best described as a moderate-intensity statin dose?
    A. Pravastatin 20 mg/day. B. Lovastatin 20 mg/day.
    C. Atorvastatin 40 mg/day. D. Rosuvastatin 10 mg/day

Questions 15 – 17 pertain to the following case

Ato MR is a 78-year-old man who presents to the emergency department for symptoms of right-sided paralysis. He states that these symptoms began about 5 hours ago and have not improved since then. He also has hypertension, BPH, DM, ED, and osteoarthritis.

15. Which is the most accurate list of MR's risk factors for stroke? .
    A. Erectile dysfunction, age, osteoarthritis.
    B. Sex, diabetes mellitus, osteoarthritis
    C. Benign prostatic hypertrophy, diabetes mellitus, age, sex.
    D. Age, diabetes mellitus, sex, hypertension.
16. Is MR a candidate for tissue plasminogen activator for treatment of stroke?
    A. Yes, he is candidate
    B. No, he is too old.
    C. No, his stroke symptoms began too long ago.
    D. No, his DM is a contraindication for tissue plasminogen activator.
17. MR was previously taking no drugs at home. Which choice is the best secondary stroke prevention therapy for this patient?
    A. Sildenafil B. Ibuprofen
    C. Aspirin D. Warfarin
18. You are the pharmacist at a community pharmacy and receive a call from Ato BM, a 60-year-old man recently given a diagnosis of atrial fibrillation. He is concerned about his risk of having a stroke because his friend, who also has atrial fibrilation, asked him which dose of warfarin he is taking. BM called you because he is not taking warfarin and wants to know whether he should. He has no other medical conditions and takes atenolol 50 mg/day orally for ventricular rate control. After encouraging BM to discuss this with his physician, what should you tell him?
    A. You need warfarin treatment to prevent a stroke.
    B. You do not need warfarin, but you should take aspirin and clopidogrel.
    C. You do not need drug therapy at this time.
    D. Because you have atrial fibrillation, nothing can reduce your risk of stroke.
19. W/ro LS is a 72-year-old woman with a medical history of hypertension, type 2 diabetes mellitus, renal failure, and atrial fibrillation. She presents to the anticoagulation clinic for her initial visit. Which best reflects her target INR?
    A. 1.5. B. 1.75. C. 2.5. D. 3.2

Question 20 & 21 pertain to the folloOwing case:

A 78-year-old man has a past medical history of hypertension for 10 years. His BP today is 158/82 mm Hg (156/84 mm Hg when repeated), heart rate is 60 beats/min, serum creatinine is 1.2 mg/dL, and potassium is 4.3 mEq/L. He is currently on lisinopril 40 mg daily and amlodipine 10 mg daily, weighs

73 kg, is 179 cm tall, smokes one pack cigarettes daily, and consumes two to three ethanol-containing drinks weekly.

20. Which of the following is the most appropriate medication to add to his antihypertensive regimen?
A. Verapamil B. Losartan
C. Hydrochlorothiazide D. Metoprolol

21. Which of the following lifestyle modifications is most reasonable to recommend in this patient to specifically lower his BP?
A. Weight loss B. Smoking cessation
C. Diet management D. Decrease alcohol intake

The following case pertains to question #22 & 23:

A 37-year-old woman has a BP measurement of 160/100 mm Hg when she first arrives for a routine physical examination by a nurse. She has no previous history of hypertension, and the only other time she had been seen by a healthcare provider, her BP was 120/80 mm Hg. She is extensively interviewed and examined, and has no signs of acute or chronic hypertension-associated end-organ damage. Her physician measures her BP again 20 minutes later, and it is 142/92 mm Hg (140/90 mm Hg when repeated). Her most recent fasting lipid panel was also normal.

22. Which of the following is the most accurate clinical assessment of her present situation?
A. Prehypertension B. Elevated blood pressure
C. Stage I hypertension D. White coat hypertension

23. Which of the following is the most appropriate BP goal in this patient?
A. <120/80 mm Hg B. <130/80 mm Hg
C. <140/90 mm Hg D. <150/90 mm Hg

The following case pertains to question #24 & 25:

A 60-year-old woman with hypertension, type 2 diabetes, and heart failure with reduced ejection fracture is seen 2 months after experiencing an acute myocardial infarction. She also has a history of dyslipidemia. Her present BP is 130/84 mm Hg (132/82 mm Hg when repeated) and her heart rate is 60 beats/min. Her serum creatinine is 1.1 mg/dL, serum potassium is 3.5 mEq/L, and spot urinalysis shows 20 mg albumin/g creatinine. She currently has no peripheral or pulmonary edema. She is taking carvedilol 25 mg BID, furosemide 40 mg BID and enalapril 20 mg twice daily.

24. Which of the following medical conditions is a compelling indication for the use of carvedilol in this patient as a first-line agent?
A. Diabetes B. Recent MI
C. CKD D. Advanced age

25. Which of the following statements is most appropriate to include when counseling this patient regarding her antihypertensive therapy?
A. It will be possible to stop enalapril once your BP is at goal.

B. Long-term benefits of these medications are a reduced risk of CV events
C. If you experience new onset depression you should stop taking carvedilol.
D. If you experience dry cough, stop taking lisinopril because this can lead to angioedema.

26. Which of the following is preferred as add-on therapy for a patient who is post-MI (1 month ago) with a BP of 146/88 mm Hg (144/86 mm Hg when repeated) while treated with metoprolol succinate 200 mg daily?
A. Hydrochlorothizide B. Verapamil
C. Amlodipine D. Lisinopril

27. Which of the following is preferred as initial antihypertensive therapy for a 63-year-old woman who is diagnosed with hypertension and has a history of ischemic stroke (6 months ago), with a BP of 186/108 mm Hg (184/106 mm Hg when repeated)?
A. A thiazide with an ACEi B. A thiazide with a nonselective β-blocker
C. A thiazide alone D. An ACEi with an ARB

28. A 52-year-old man has chronic stable angina and hypertension. He is experiencing ischemic chest pain twice weekly while being treated with metoprolol succinate 100 mg daily. His BP is 146/90 mm Hg (144/92 mm Hg when repeated), and heart rate is 58 beats/min. Which of the following is the most appropriate agent to add in this patient?
A. Lisinopril 20 mg daily B. Diltiazem SR 180 mg daily
C. Amlodipine 5 mg daily D. Irbesartan 150 mg daily

29. A patient with newly diagnosed hypertension asks you for advice lifestyle modifications to lower BP. Which of the following is/are appropriate recommendations?
A. Decrease your dietary intake of table salt and processed foods.
B. Increase your daily ingestion of red meat.
C. Start 45 to 60 minutes of vigorous exercise daily.
D. Decrease your daily fiber intake

30. A 32-year-old woman with hypertension wishes to become pregnant. Her physician informs her that she will have to switch to another antihypertensive drug. Which of the following drugs is absolutely contraindicated in pregnancy?
A. Atenolol B. Losartan C. Methyldopa D. Nifedipine

31. A patient with hypertension and angina is referred for treatment. Metoprolol and verapamil are among the drugs considered. Both metoprolol and verapamil are associated with which one of the following?
A. Hypoglycemia B. Increased PR interval
C. Tachycardia D. Thyrotoxicosis

32. Which of the following is correct about the pharmacotherapy of HFpEF?
    - A. Beta-blockers reduce mortality
    - B. Beta-blocker therapy can be used safely in this population but does not improve mortality
    - C. ACE inhibitors are the only agents that have been shown to reduce mortality in the HFpEF population
    - D. Beta-blocker therapy is contraindicated in patients with HFpEF.
33. Which of the following adverse effects of enalapril can be avoided by switching to candesartan?
    - A. Fetal toxicity
    - B. Renal insufficiency
    - C. Hyperkalemia
    - D. Cough
34. Which of the following medications can exacerbate HFrEF?
    - A. Metformin
    - B. Diltiazem
    - C. Rosuvastatin
    - D. Amiodarone
35. Which of the following should be used to monitor loop diuretic therapy in patients with heart failure?
    - A. Daily weights, serum potassium, serum magnesium
    - B. Thyroid stimulating hormone (TSH) and free T4
    - C. Hemoglobin A1C and fasting blood sugar
    - D. Fasting lipid profile
36. A patient with a history of hypertension was recently diagnosed with Stage C HFrEF. Current medications include sustained release diltiazem 180 mg QD, digoxin 0.125 mg QD, and furosemide 40 mg QD. The patient's vital signs are currently: BP 145/90 and pulse 68 BPM. Which of the following changes should be recommended in this patient's drug therapy?
    - A. Change diltiazem to verapamil
    - B. Add torsemide
    - C. Discontinue diltiazem and initiate enalapril
    - D. Add propranolol to the present therapy
37. A 63-year-old female with stage C HFrEF is currently taking enalapril 5 mg twice daily, furosemide 40 mg twice daily, digoxin 0.125 mg qd, and metoprolol succinate 25 mg daily. Today, she presents with increasing shortness of breath, fatigue, and ankle swelling. She also reports an 4kg weight gain over the past week. Her labs are significant for serum potassium of 5.2 mEq/L and serum creatinine of 2.2 mg/dL. Which of the following interventions is most appropriate?
    - A. Increase the dose of furosemide to 80 mg bid
    - B. Increase the dose of metoprolol to 50 mg qd
    - C. Start spironolactone 12.5 mg qd
    - D. Increase the dose of digoxin to 0.25 mg qd

38. After your patient has been receiving digoxin for 3 weeks, he presents to the emergency department with an arrhythmia. Which one of the following is most likely to contribute to the arrhythmogenic effect of digoxin?
    A. Increased parasympathetic discharge
    B. Increased intracellular calcium
    C. Decreased sympathetic discharge
    D. Decreased intracellular ATP
    E. Increased extracellular potassium
39. A patient who has been taking digoxin for several years for atrial fibrillation and chronic heart failure is about to receive atropine for another condition. A common effect of digoxin (at therapeutic blood levels) that can be almost entirely blocked by atropine is
    A. Headaches B. Increased atrial contractility
    C. Increased PR interval on ECG D. Tachycardia
40. A 72-year-old woman has long-standing heart failure. Which one of the following drugs has been shown to reduce mortality in chronic heart failure?
    A. Atenolol B. Digoxin
    C. Furosemide D. Spironolactone
41. A 68-year-old man with a history of chronic heart failure goes on vacation and abandons his low-salt diet. Three days later, he develops severe shortness of breath and is admitted to the local hospital emergency department with significant pulmonary edema. The first-line drug of choice in most cases of acute decompensation in patients with chronic heart failure is
    A. Digoxin B. Enalapril C. Furosemide D. Metoprolol
42. Which of the following has been shown to prolong life in patients with chronic congestive failure in spite of having a negative inotropic effect on cardiac contractility?
    A. Carvedilol B. Digoxin C. EnalapriL D. Furosemide
43. Which of the following vitamin K dependent clotting factors has the shortest half-life?
    A. Factor X B. Factor IX C. Factor VII D. Factor II
44. A 70-year-old male patient with DVT and a baseline INR of 1.1 is started on warfarin 5 mg daily on day 1 and day 2 as well as enoxaparin 80 mg SC BID. He has no history of malignancy, malnutrition, heart failure, alcohol abuse, or liver dysfunction. His INR today (Day 3) is 1.5. Select the best warfarin dose for Day 3:
    A. 10 mg B. 5 mg
    C. 1 mg D. Hold warfarin today
45. A female patient is confused about what her INR result means. Which one of the following statements best describes what she needs to understand about her INR results?

A. When the INR is below 2.0 she is at increased risk for bleeding.
B. When the INR is between 2 and 3 she can continue the same dose of warfarin
C. When the INR is below 2.0 her dose of warfarin may need to be adjusted.
D. When the INR is higher than 3.0 she is at increased risk for having another VTE.

46. A patient's INR is 1.6 following a significant dietary change. Which of the following is the most likely explanation for today's lab result?
A. Eating more green leafy vegetables than usual
B. Eating fewer green leafy vegetables than usual
C. Drinking grapefruit juice
D. Taking fatty foods

47. Which of the following is not a risk factor for DVT in hospitalized patients?
A. Cancer B. Hypertension
C. Age >70 years D. Estrogen therapy

48. Which one of the following states is the most potent LDL lowering drug?
A. Lovastatin B. Pravastatin
C. Rosuvastatin D. Simvastatin

49. All of the following are considered to be CHD risk equivalents except,
A. Asthma B. Diabetes
C. Symptomatic carotid artery disease D. Peripheral arterial disease

50. A 45-year-old woman with hyperlipidemia and frequent migraine headaches develops angina of effort. Which of the following is relatively contraindicated because of her migraines?
A. Diltiazem B. Metoprolol C. Nitroglycerin D. Verapamil

51. Certain drugs can cause severe hypotension when combined with nitrates. Which of the following interacts with nitroglycerin by inhibiting the metabolism of cGMP?
A. Atenolol B. Nifedipine
C. Enalapril D. Sildenafil

52. Which of the following would result in underestimation of the BP?
A. Using a cuff that is too small
B. Using a cuff that is too large
C. Consumption of caffeine within 30 minutes of BP measurement
D. Exercise within 30 minutes of BP measurement

53. Which of the following would be a first-line drug of choice for a patient who has HTN and history of diabetes mellitus?
A. Lisinopril B. Amlodipine
C. Metoprolol D. Hydrochlorothiazide

54. Which of the following medication combinations is the most appropriate for treatment of HTN in a patient with no compelling indications?